UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,996	02/05/2007	Michiel T. Kreutzer	63611A	6871

109 7590 12/17/2010

The Dow Chemical Company
P.O. BOX 1967
2040 Dow Center
Midland, MI 48641

EXAMINER	
HANLEY, SUSAN MARIE	
ART UNIT	PAPER NUMBER
1651	

NOTIFICATION DATE	DELIVERY MODE
12/17/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

FFUIMPC@dow.com

Office Action Summary	Application No.	Applicant(s)	
	10/589,996	KREUTZER ET AL.	
	Examiner	Art Unit	
	SUSAN HANLEY	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-13 and 17-20* is/are pending in the application.

4a) Of the above claim(s) *9,19 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-8, 10-13, 17 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of the specie of claim 8, wherein the catalyst is an enzyme, in the reply filed on 06/01/2009 is again acknowledged. The restriction requirement for the specie wherein the catalyst is carbon was withdrawn since an enzyme is comprised of carbon. Claims 9, 19 and 20 stand withdrawn.

Claims 1, 3-8, 10-13, 17 and 18 are under examination.

Withdrawal of Rejections

Applicant's arguments, filed 10/14/2010, have been fully considered regarding previous rejections have been fully considered and they are partially persuasive. Rejections and/or objection not reiterated from previous Office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim 1 is directed to a method for forming a reaction product by flowing a reactant into a ceramic honeycomb having an inlet and outlet that are connected by adjacent channels having thin porous walls such that the liquid substantially penetrates the into the walls and the reactant reacts as the liquid containing the reactant flows from the inlet to the outlet of the monolithic ceramic honeycomb and recovering the product

from the outlet end of the ceramic honeycomb. The porosity of the partition walls is at least 50% and the mean pore size is at least 5 micrometers to at most 10 micrometers (new limitation). The ceramic honeycomb is acicular ceramic having an aspect ratio of at least about 2. Claim 8 is directed to the elected specie, an enzyme. Claim 18 is directed to a catalyst comprising carbon. Claims 12 and 13 are directed to using a solvent that is water. Claims 3-7 recite that the liquid containing the reactant penetrates in an amount that is at least 10% of the static liquid fraction as determined using the resident time distribution obtained under Taylor flow of a tracer pulsed into the liquid (claim 3); that the amount in claim 3 is at least about 15% of the static liquid fraction (claim 4); that the method has a mass exchange as calculated using an E-curve at is at least about 0.4 % (claim 5); that the mass exchange is at least about 0.7 (claim 6) or that the static liquid fraction is at least about 1.25 (claim 7).

van den Broecke teaches that fermentation processes involve the culturing of microorganisms, including yeast, and require a supply of oxygen for the aerobic metabolism of said microorganisms. Hence, oxygen is a reactant since the microorganisms require it for the fermentation process (instant claim 10). Usually the oxygen is supplied by passing an oxygen-containing gas such as air, though the liquid in the fermentation vessel. The oxygen is transferred from the gas bubbles (instant claim 11) to the liquid phase thus allowing its uptake by the microorganism (page 1, lines 6-14).

Claims 1, 3-8, 12, 13, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duncombe et al (US 4,430,348) in view of Asai et al. (English

translation of JP 62134089; "Asai"; new reference) and Shiraishi (Hei 5-273119; cited in the IDS filed 1/22/07; translation).

Duncombe discloses a method for the production of a super-attenuated low calorie beer that is produced by fermenting beer though glucoamylase immobilized on a ceramic monolith. The glucoamylase is immobilized on the carrier via covalent bonds (abstract of the patent; instant claim 8, the specie for the catalyst is an enzyme; it is disposed on the ceramic surface as in instant claim 1). The limit dextrins (the reactants) are hydrolyzed by the immobilized glucoamylase by passing the beer through said monolith which is porous (see figure 2; lines 7 of instant claim 1) such that the limit dextrins come into contact with said glucoamylases that are immobilized on the ceramic surface (claim 1 of the patent). The reactor consists of a ceramic monolith having a number of discrete openings or cells within an external core. For enzyme immobilization, the maximum surface area (large number of small cells per unit cross-section) is desired so that the maximum amount of enzyme can be attached and the reactor size can be minimized (col. 5, lines 25-36).

The reactor consists of an enzyme reactor tank having a cylindrical main body in which the ceramic monolith is disposed. The tank has a inlet at the bottom and an outlet at the top (hence it is a flow through apparatus, as required by instant claim 1). The enzyme reactor is positioned next to and is in liquid communication with a fermentation tank (col. 7, lines 30-65). In use, the fermenting beer which contains suspended yeast cells is pumped from the fermentation tank into the enzyme reactor and back to the fermentation tank. Hence, the fermentation tank receives the products

of the enzyme reactor and therefore said products are recovered from the reactor tank that contains the immobilized enzyme, as in instant claim 1, part (b). The liquid is beer which contains water as in instant cams 12 and 13.

Duncombe does not teach that the structure of the cells is a honeycomb, that the ceramic honeycomb is an acicular ceramic such as acicular mullite having an aspect ratio of at least about 2, wherein partition walls have a porosity of at least 50% and the mean pore size of at least 5 micrometers. Nor does Duncombe teach that the liquid containing the reactant penetrates in an amount that is at least 10% of the static liquid fraction as determined using the resident time distribution obtained under Taylor flow of a tracer pulsed into the liquid (claim 3); that the amount in claim 3 is at least about 15% of the static liquid fraction (claim 4); that the method has a mass exchange as calculated using an E-curve at is at least about 0.4 % (claim 5); that the mass exchange is at least about 0.7 (claim 6) or that the static liquid fraction is at least about 1.25 (claim 7).

Asai discloses a method for making a product from a reactant wherein the reactant in a liquid flow is dispersed through a ceramic honeycomb structure having numerous pores and pluralities of through-holes (Example 3, line 21 to page 14, line 2). Microorganisms (which contain enzymes) are immobilized on honeycomb (Claim 1 on p. 2 of the translation). The average pore size of the partition wall of the ceramic honeycomb is 10 to 100 μM (p. 2, claim 2 of the translation). The disclosure of 10 μM and 100 μM for the pore sizes are species that anticipate the claimed range of at least about 5 μM to at most 100 μM (new limitation in claim 1). 100 μM meets the newly

claimed upper range of at most 100 μM in amended claim 1. The values between 10 and 100 μM are species within the prior art which suggest the same values as claimed. It is noted that the grounds of rejection have not changed even in view of the new limitation of "at most 100 micrometers " since 100 micrometers was previously cited as anticipating the previously claimed range.

In example 3 (p. 13 of the translation, line 14), Asai teaches that the average pore size of the ceramic honeycomb reactor was 50 μM, thus anticipating the claimed range of at least 5 μM. The porosity of the honeycomb structure is 30-70% (p. 2 of the translation, claim 3). The disclosure of 70%, the upper end of the disclosed range, is a species that anticipates the claimed range. The disclosure motivates the claimed value of at least 50%. The values between 50% and 70% are species within the prior art which suggest the same values as claimed. In example 3, Asai discloses that the porosity of the bioreactor is 50% (line 13, page 13 of the translation), a specie that anticipates the claimed range of at least 50%. Asai teaches that the advantage of using a bioreactor having the disclosed elements is that the microorganisms/enzymes lose less activity during the immobilization process of the microorganism and provides for a large contact area between the microorganism and the substrate (p. 5, lines 18-25). Asai also teaches that the reactor can be made from mullite (p. 7 of the translation, line 6).

Shiraishi teaches that mullite is suitable for the attachment of enzymes or microorganisms or enzymes for such a carrier. Chitosan film (a polysaccharide) is easily bonded to the ceramic carrier with strong adhesion in order to support the

microorganism or enzyme (page 2 of the translation, under the heading "Constitution"). The mullite is an a turf-like state that is grown from needle (acicular) crystals in a highly dense state (page 2 of the translation under claim 2). The resulting ceramic carrier can support a thin film which is outstanding for the permeability of liquids (page 4, paragraph [0004]. Glucoamylase was successfully attached to said acicular mullite covered with chitosan. The fixed enzyme converted starch into glucose (Example 3, page 5 of the translation). The acicular mullite crystals are 1-100 μm long and 0.1 to 10 μm thick (page 2, Constitution and claim 2). The aspect ratio (length divided by thickness (width)) of the end points is 1/0.1 and 100/10 which are both a ratio of 10:1. This is a specie that anticipates the claimed range. The ratio of the lowest length value to the highest width value is 1/10 or 0.1/1. The ratio of the highest length value to the lowest width value is 100/0.1 or 1000/1. This provides an aspect ratio range of 0.1/1 to 1000/1. The ratio value of 1000/1 is a specie that anticipates the claimed range. The generic disclosure suggests or motivates the specific value, an aspect ration of 2, which is the lower end of the claimed range. The values between 2 and 1000/1 are species within the prior art which suggest the same values as claimed.

Shiraishi also discloses that there are a number of ways to fix enzymes and microorganisms onto bioreactors including covalent bonding. Covalent bonding has the problem that the microorganism is markedly modified or degraded by the fixation process, thus leading to a decline in the activity for the reaction. Another problem of covalent bonding is that the amount of enzyme that can be fixed is limited (page 3 of the translation paragraph [0003]).

It would have been obvious to one of ordinary skill in the art, a biochemist, at the time the invention was made to use a honeycomb ceramic in the method of Duncombe. The ordinary artisan would have been motivated to do so because the honeycomb structure optimizes the surface area thus guaranteeing a large contact area and the pore size and porosity range allows for less loss of actiivty during the immobilization process of the microorganism. The use of the honeycomb structure would naturally allow for the penetration of the liquid containing the reactant, limit dextrin, to flow from the inlet to the outlet, thus, undergoing reaction (instant claim1, regarding the penetration of the liquid into the walls of the honeycomb). The ordinary artisan would have had a reasonable expectation that enzymes immobilized on a honeycomb ceramic monolith would successfully carry of the desired glucoamylase reaction because Asai demonstrates that microorganisms which are immobilized in this manner have the desired activities (Example 3). The ordinary artisan would have known from the combined references that microorganisms and enzymes can both be immobilized on ceramic surfaces for the purpose of catalyzing biochemical reactions.

It would have been obvious to one of ordinary skill in the art, a biochemist, at the time the invention was made to made to make the pore size and the porosity of the partition walls of the ceramic honeycomb reactor disclosed by the combination of Asai and Duncombe at least 10-100 micrometers and at least 50%-70%, respectively. The ordinary artisan would have been motivated to do so because Asai teaches that ceramic honeycomb reactors having said pore size and porosity ranges have the advantage of causing less loss of activity during the immobilization process and providing for large

contact area between the microorganism and the substrate. The ordinary artisan would have had a reasonable expectation that said average pore size and porosity ranges an would be successful in the combined method of the Duncombe and Asai because the reactor taught by Asai has the same set up as that of the combined references: a ceramic honeycomb reactor having pores with microorganisms immobilized thereon.

It would have been obvious to one of ordinary skill in the art, a biochemist, to make the honeycomb ceramic of the combined references of Asai and Duncombe out of acicular mullite having an aspect ratio of 10/1 or 2 to 1000/1. The ordinary artisan would have known from Shiraishi that microorganisms, like enzymes can be fixed onto ceramics via a polysaccharide. The ordinary artisan would have been motivated to adhere the enzymes of the combined references to a honeycomb reactor comprising mullite having said aspect ratio because the adhesion of microorganisms via a polysaccharide to the acicular mullite provides a dense surface that supports the microorganisms which is outstanding for the permeability of liquids. The ordinary artisan would have had a reasonable expectation that the microorganisms would be active when attached to acicular mullite having said aspect ratio because Shiraishi teaches that fixed glucoamylase was able to convert starch into glucose (Ex. 3) Kobayashi teaches that microorganisms attached to ceramics are active.

Regarding the limitations of claims 3-7, said limitations naturally flow from the factors of pore size and porosity of the monolithic ceramic honeycombed reactor since said factors govern the flow of a liquid through a honeycomb structure. In this case, the burden is shifted to Applicant to distinguish the claimed invention from the cited prior art.

It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Response to Arguments

Applicants argue that there is no substantive difference in Duncombe compared to Kobayashi other than Duncombe describes bubbling gas through the monolith. Applicants assert that the same requirements in claims 1 and 3-6 are lacking in Duncombe as in Kobayashi for the same reasons even when combined with Asai and/or Shiraishi.

Regarding Kobayashi, Applicants argue that the solidified gel will obstruct any pores within the ceramic honeycomb wall and that there can be no penetration of the reactants into the walls of the ceramic honeycomb as describes by Asai. Applicants assert that the pores of Asai are also filled (p. 8, last full paragraph) and that this teaches away from the claimed invention since claim 1 requires that the reactants penetrate the walls of the ceramic honeycomb. Applicants argue that the combination of Kobayashi and Asai teach away from the claimed invention since the pores would be filled or obstructed by the catalyst layer and no penetration would occur.

Applicants agree that Shiraishi describes that the mullite would be in a highly dense state. Applicants assert that the mullite in practical Example 2 has pores that are

0.1 to 1 micrometer and that the film deposited on them is from 10 to 100 micrometers thick. Applicants conclude that the coating thickness would obstruct any pores of the highly dense mullite layer and there would be no penetration of the reactant into the walls as required by claim 1 and its dependent claims.

Applicants' arguments regarding Kobayashi were persuasive and the rejections based on Kobayashi were withdrawn. However, Applicants' arguments regarding obstruction of the pores of the combined references of Duncombe, Asai and Shiraishi are deemed not persuasive.

The pores size range disclosed by Asai is 10 to 100 micrometers. Shiraishi discloses that the acicular mullite crystals are 1-100 μm long and 0.1 to 10 μm thick and adhere to the ceramic honeycomb (page 2, Constitution and claim 2). Using the lower end of the length and width of the crystals, 1 μm and 0.1 μm respectively, the crystals adhered onto the honeycomb structure of Asai would not obstruct the pores since the pores are a minimum of 10 μm to a maximum of 100 μm which exceeds crystals having a length and width of 1 μm and 0.1 μm, respectively. Thus, even with a coating of crystals, there is still plenty of room for flow through of reactants through the pores. Asai clearly discloses that the yeast-immobilized honeycomb has the through-holes (p. 11, third paragraph) with a shorter opening length than a conventional honeycomb structure which leads to a larger effective surface area per unit volume and a better yield of ethanol. Thus, Asai et al. envision a honeycomb with yeast immobilized on it such that there are still though holes in the walls through which reactants can flow to

react with the yeast disposed thereon. Hence, the ordinary artisan would not want to block the pores with the adhered mullite.

Regarding the pore size of the crystals, this is not relevant because the pore size of the crystals themselves are not the same thing as the size of the pores in the walls. That is, the crystals may have pores but they are adhered to the pores such that pores are still present in the walls (see the response in the previous paragraph).

A film of 10 to 100 μm thick of microorganisms is still within the range of keeping the pores open. Using upper end of the pore size of Asai (100 μm) and the lower end of the film thickness taught by Shiraishi (10 μm) if a pore having a diameter of 100 μm was coated all around the surface of the pore with 10 μm of film, it would results in a net pore diameter of 80 μm which is a specie that meet the claimed range of at least 5 up to 100 μm. Furthermore, Asai clearly teaches that pores are maintained in the walls of the honeycomb structure after the yeast is immobilized on the walls. On page 11 of the translation, Asai teaches that the disclosed bioreactor produces more ethanol compared to standard bioreactors because the yeast is immobilized to the ceramic honeycomb structure which has the through-holes with a shorter opening length than a conventional honeycomb structure. This leads to a larger effective surface area per unit volume. Thus, Asai et al. envision a honeycomb with yeast immobilized on it such that there are still though holes in the walls through which reactants can flow to react with the yeast disposed thereon.

Responding to Applicants' arguments that the microorganisms fill the pores (p. 8 of the Asai translation), Asai is referring to the manufacture of the microorganism

adhered honeycomb. The pores are filled with with microorganisms during the cultivation by shaking. This is evidenced in Ex. 1 on p. 9 in the second full paragraph which describes the immobilization of the microorganisms to the honeycomb structure. The honeycomb structure was subjected to deareation so that the solution of the microorganisms permeate the pores and then by shaking, the microorganisms are immobilized onto the honeycomb structure. Asai then teaches the length of the opening of the through-holes, the porosity and the average pore size of the structure after this procedure in Table 1.

On page 11 of the translation, Asai teaches that the disclosed bioreactor produces more ethanol compared to standard bioreactors because the yeast is immobilized to the ceramic honeycomb structure which has the through-holes with a shorter opening length than a conventional honeycomb structure. This leads to a larger effective surface area per unit volume. Thus, Asai et al. envision a honeycomb with yeast immobilized on it such that there are still though holes in the walls through which reactants can flow to react with the yeast disposed thereon.

Claims 1, 3-8, 12, 13, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duncombe et al (US 4,430,348) in view of Asai et al. (English translation of JP 62134089; "Asai"; new reference) and Shiraishi (Hei 5-273119; cited in the IDS filed 1/22/07; translation), as applied to claims 1, 3-8, 12, 13, 17 and 18 above, and further in view of van den Broecke et al. (WO 02/33048) for the reasons stated in the last Office action and as given herein.

Applicants did not specifically argue against this rejection. Hence, the rejection is maintained for the reasons of record.

Claims 1, 3-8, 10-13, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Asai et al. (English translation of JP 62134089; "Asai"; new reference) in view of Shiraishi (Hei 5-273119; cited in the IDS filed 1/22/07; translation).

Asai discloses a method for making a product from a reactant wherein the reactant in a liquid flow is dispersed through a ceramic honeycomb structure having numerous pores and pluralities of through-holes (Example 3, line 21 to page 14, line 2; meeting the limitation in claim 1 of a plurality of channels defined by a plurality of interlaced porous partition walls). In Example 3, *Acetobacter aceti* (having enzymes as in instant claims 8 and 18) was suspended in a precultivation media with a cordierite ceramic honeycomb structure having a porosity of 50% and an average pore size of 50 μm. These are species that anticipate the claimed ranges of a porosity of 50% and at least a pore size of 5 μm, respectively in instant claim 1. At page 14, last paragraph, Asai teaches that the process absorbs the bacteria onto the surface of the ceramic honeycomb structure, meeting the limitation of having a catalyst disposed thereon in instant claim 1). The obtained bioreactor element was place in a reactor tube. The pre-cultivation solution (instant claims 12 and 13) was introduced from the bottom of the reactor with air at the same time (instant claims 10 and 11; microorganisms need the oxygen in air to survive). The concentration of the acetic acid was measured at the

reactor exit (instant claim 1, part (b)). Hence, the liquid flows from an entrance to an exit, as in instant claim 1 (a). Asai teaches that the method using the ceramic honeycomb structure produced a higher concentration of product compared to bacteria that was inclusion-immobilized in a bead using sodium alginate.

Asai also teaches that the average pore size of the partition wall of the ceramic honeycomb is 10 to 100 μM (p. 2, claim 2 of the translation). The disclosure of 10 and 100 micrometers for the pore size are species that anticipate the claimed range of at least 10 μM to at most 100 μM (new limitation). The values between 10 and 100 μM are species within the prior art which suggest the same values as claimed. The porosity of the honeycomb structure is 30-70% (p. 2 of the translation, claim 3). The disclosure of 70%, the upper end of the disclosed range, is a species that anticipates the claimed range. The disclosure motivates the claimed value of at least 50%. The values between 50% and 70% are species within the prior art which suggest the same values as claimed. Asai also teaches that the reactor can be made from mullite (p. 7 of the translation, line 6). It is noted that the grounds of rejection have not changed even in view of the new limitation since 100 micrometers was previously cited as anticipating the previously claimed range.

Asai does not teach that ceramic honeycomb is an acicular ceramic such as acicular mullite having an aspect ratio of at least about 2. Nor does Asai teach that the liquid containing the reactant penetrates in an amount that is at least 10% of the static liquid fraction as determined using the resident time distribution obtained under Taylor flow of a tracer pulsed into the liquid (claim 3); that the amount in claim 3 is at least

about 15% of the static liquid fraction (claim 4); that the method has a mass exchange as calculated using an E-curve at is at least about 0.4 % (claim 5); that the mass exchange is at least about 0.7 (claim 6) or that the static liquid fraction is at least about 1.25 (claim 7).

The disclosure by Shiraishi is discussed supra. Shiraishi also discloses that physical absorption of enzymes to a reactor has drawbacks because the enzyme was apt to peel from the carrier during the reaction because of weak adhesion between the carrier and the enzyme.

It would have been obvious to one of ordinary skill in the art, a biochemist, to employ a ceramic honeycomb of acicular mullite having an aspect ratio of 10/1 or 2 to 1000/1, wherein the microorganisms are adhered to the mullite by a polysaccharide in the method of Asai. The ordinary artisan would have known from Shiraishi that microorganisms, like enzymes can be fixed onto ceramics via a polysaccharide. The ordinary artisan would have been motivated to adhere the microorganisms of Asai a honeycomb reactor comprising mullite having said aspect ratio because the adhesion of microorganisms via a polysaccharide to the acicular mullite provides a dense surface that supports the microorganisms which is outstanding for the permeability of liquids. The ordinary artisan would have had a reasonable expectation that the microorganisms would be active when attached to acicular mullite having said aspect ratio because Shiraishi teaches that fixed glucoamylase was able to convert starch into glucose and Asai teaches that microorganisms attached to ceramics are active.

Regarding the limitations of claims 3-7, said limitations naturally flow from the factors of pore size and porosity of the monolithic ceramic honeycombed reactor since said factors govern the flow of a liquid through a honeycomb structure. In this case, the burden is shifted to Applicant to distinguish the claimed invention from the cited prior art. It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Response to Arguments

Applicants argue that Asai in view of Shiraishi both describe filling or obstructing the pores of the honeycomb ceramic such that the reactants would not penetrate the wall of the honeycomb as required in claim 1.

Applicants argument has been considered but it is non-persuasive.

Applicants' arguments regarding Kobayashi were persuasive and the rejections based on Kobayashi were withdrawn. However, Applicants' arguments regarding obstruction of the pores of the combined references of Asai and Shiraishi are deemed not persuasive.

The pores size range disclosed by Asai is 10 to 100 micrometers. Shiraishi discloses that the acicular mullite crystals are 1-100 μm long and 0.1 to 10 μm thick and adhere to the ceramic honeycomb (page 2, Constitution and claim 2). Using the lower

end of the length and width of the crystals, 1 μm and 0.1 μm respectively, the crystals adhered onto the honeycomb structure of Asai would not obstruct the pores since the pores are a minimum of 10 μm to a maximum of 100 μm which exceeds crystals having a length and width of 1 μm and 0.1 μm, respectively. Thus, even with a coating of crystals, there is still plenty of room for flow through of reactants through the pores. Asai clearly discloses that the yeast-immobilized honeycomb has the through-holes (p. 11, third paragraph) with a shorter opening length than a conventional honeycomb structure which leads to a larger effective surface area per unit volume and a better yield of ethanol. Thus, Asai et al. envision a honeycomb with yeast immobilized on it such that there are still though holes in the walls through which reactants can flow to react with the yeast disposed thereon. Hence, the ordinary artisan would not want to block the pores with the adhered mullite.

Regarding the pore size of the crystals, this is not relevant because the pore size of the crystals themselves are not the same thing as the size of the pores in the walls. That is, the crystals may have pores but they are adhered to the pores such that pores are still present in the walls (see the response in the previous paragraph).

A film of 10 to 100 μm thick of microorganisms is still within the range of keeping the pores open. Using upper end of the pore size of Asai (100 μm) and the lower end of the film thickness taught by Shiraishi (10 μm) if a pore having a diameter of 100 μm was coated all around the surface of the pore with 10 μm of film, it would results in a net pore diameter of 80 μm which is a specie that meet the claimed range of at least 5 up to 100 μm. Furthermore, Asai clearly teaches that pores are maintained in the walls of the

honeycomb structure after the yeast is immobilized on the walls. On page 11 of the translation, Asai teaches that the disclosed bioreactor produces more ethanol compared to standard bioreactors because the yeast is immobilized to the ceramic honeycomb structure which has the through-holes with a shorter opening length than a conventional honeycomb structure. This leads to a larger effective surface area per unit volume. Thus, Asai et al. envision a honeycomb with yeast immobilized on it such that there are still though holes in the walls through which reactants can flow to react with the yeast disposed thereon.

Responding to Applicants' arguments that the microorganisms fill the pores (p. 8 of the Asai translation), Asai is referring to the manufacture of the microorganism adhered honeycomb. The pores are filled with microorganisms during the cultivation by shaking. This is evidenced in Ex. 1 on p. 9 in the second full paragraph which describes the immobilization of the microorganisms to the honeycomb structure. The honeycomb structure was subjected to deareation so that the solution of the microorganisms permeate the pores and then by shaking, the microorganisms are immobilized onto the honeycomb structure. Asai then teaches the length of the opening of the through-holes, the porosity and the average pore size of the structure after this procedure in Table 1.

On page 11 of the translation, Asai teaches that the disclosed bioreactor produces more ethanol compared to standard bioreactors because the yeast is immobilized to the ceramic honeycomb structure which has the through-holes with a shorter opening length than a conventional honeycomb structure. This leads to a larger effective surface area per unit volume. Thus, Asai et al. envision a honeycomb with

yeast immobilized on it such that there are still though holes in the walls through which reactants can flow to react with the yeast disposed thereon.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSAN HANLEY whose telephone number is (571)272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sandra Saucier/
Primary Examiner, Art Unit 1651

/Susan Hanley/
Examiner, Art Unit 1651